Heart Failure Pharmacotherapy

Based on the 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure and the 2023 ACC Expert Consensus Decision Pathway on Management of HFpEF

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References:
[1] Classes of Heart Failure. American Heart Association. May 31, 2017. https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure/classes-of-heart-failure
[2] Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines [published correction appears in Circulation. 2022 May 3;145(18):e1033]. Circulation. 2022;145(18):e895-e1032. doi:10.1161/CIR.0000000000001063
[3] Kittleson M, Panjrath G, et al. 2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure With Preserved Ejection Fraction. J Am Coll Cardiol. 2023. doi:10.1016/j.jacc.2023.03.393

Heart Failure Categories

Stage

A
At risk for HF
- No HF signs/symptoms
- No structural/functional heart disease
- No abnormal biomarkers

B
Pre-HF
- No HF signs/symptoms
- **ONE** of the following:
  (1) Structural heart disease
  (2) ↑ filling pressures
  (3) Risk factors **PLUS** ↑ natriuretic peptides **OR** persistently ↑ cardiac troponin w/o competing diagnosis

C
Symptomatic HF
- Structural heart disease **AND**
- Current or previous HF symptoms

D
Advanced HF
- HF symptoms interfering with normal activity and/or recurrent HF hospitalizations (despite GDMT)

LVEF

HFrEF *(reduced EF)* — **LVEF ≤ 40%**

HFimpEF *(improved EF)* — **LVEF > 40%** *(upon follow up after a previous measurement of LVEF ≤ 40%)*

HFmrEF *(mildly reduced EF)* — **LVEF 41-49%** *(w/ evidence of spontaneous/provokable ↑ LV filling pressures)*

HFpEF *(preserved EF)* — **LVEF ≥ 50%** *(w/ evidence of spontaneous/provokable ↑ LV filling pressures)*

NYHA Class

I
- No symptoms from ordinary daily activities

II
- No symptom at rest
- Ordinary daily physical activities cause HF symptoms

III
- No symptom at rest
- Activities lighter than ordinary daily physical activities cause HF symptoms

IV
- Symptoms at rest
- Discomfort worsens with physical activities

Goals of Therapy

Stage A
- Primary prevention of heart failure

Stage B
- Prevention of clinical heart failure

Stage C
- Reduction of mortality
- Reduction of heart failure symptoms and hospitalization risk
- Elimination of potential barriers to self-care

Stage D
- Provision of inotropic support until mechanical circulatory support or cardiac transplantation is available
- Palliative symptom control and functional improvement (if not eligible for mechanical circulatory support or cardiac transplantation)

Pharmacotherapy Recommendations

Stage A
- Control BP in patients with hypertension
- SGLT2i in patients with T2DM **plus:**
  - Established CVD **or,**
  - High CV risk
- Manage existing comorbidities

Stage B
- ACEi and evidence-based BB in patients with LVEF ≤ 40%
  - If LVEF ≤ 40% **and recent MI**, use ARB if ACEi is not tolerated

Stage C (HFpEF)
- SGLT2i in **all patients** with HFpEF *(unless contraindicated)*
- May consider MRA and/or ARNi if LVEF < 55-60%
  - May consider regardless of LVEF for female patients
  - May consider ARB if unable to receive ARNi therapy
- PRN loop diuretic

Stage C (HFmrEF)
- PRN diuretics (**loop** preferred)
- SGLT2i may be beneficial
- May consider MRA, ACEi/ARB/ARNi, and evidence-based BB *particularly* if LVEF is closer to **HFrEF threshold**

Stage C (HFimpEF)
- Continue GDMT
  - Even if asymptomatic

Stage C (HFrEF)

All patients
- **ARNi** or **ACEi** or **ARB**
  - ARNi: NYHA class II-III
  - ACEi or ARB: NYHA class II-IV
  - Order of preference: ARNi > ACEi > ARB
  - **36-hour washout** required when switching between ACEi and ARNi (and vice versa)
- **Beta Blocker** (evidence-based)
  - Bisoprolol, carvedilol, metoprolol succinate
- **MRA** (e.g. eplerenone, spironolactone)
  - NYHA class II-IV
  - eGFR > 30 mL/min/1.73m2
  - Serum potassium < 5 mEq/L
- **SGLT2i**
  - With or without T2DM
- **Diuretics** (as needed)
  - Loop diuretics preferred

Specific patients
- **Hydralazine + isosorbide dinitrate**
  - African American patients on optimal therapy
  - NYHA class III-IV
- **Ivabradine**
  - NYHA class II-III and LVEF **≤ 35%**
  - On GDMT including **max tolerated BB**
  - NSR with resting HR ≥ 70 BPM
- **Vericiguat**
  - NYHA class II-IV and LVEF **< 45%**
  - Recent HF worsening
  - ↑ BNP or NT-proBNP
- **Digoxin**
  - If symptomatic despite GDMT **or**
  - Unable to tolerate GDMT
- **Potassium binders**
  - e.g., **Patiromer**, **sodium zirconium cyclosilicate**
  - Patients with hyperkalemia (K+ ≥ 5.5 mEq/L) while on RAASi
- **Omega-3 PUFA** (may consider as an adjunct)
  - NYHA class II-IV

Selected Medications That May Cause or Exacerbate HF

COX inhibitors (e.g., NSAIDs)	• ↑ H2O retention, ↑ vascular resistance, ↓ response to diuretics • **Immediate** onset, **major** induction/precipitation of HF
Thiazolidinediones	• Potential blockage of calcium channel • **Intermediate** onset, **major** induction/precipitation of HF
Saxagliptin, Alogliptin	• Mechanism is unclear • **Immediate or delayed** onset, **major** induction/precipitation of HF
Flecainide, Disopyramide	• Proarrhythmic, negative inotropic effects • **Immediate to intermediate** onset, **major** induction/precipitation of HF
Sotalol	• Proarrhythmic effects, beta blockade • **Immediate to intermediate** onset, **major** induction/precipitation of HF
Dronedarone	• Negative inotropic effects • **Immediate to intermediate** onset, **major** induction/precipitation of HF
Doxazosin	• Beta-1 stimulation, ↑ renin and aldosterone • **Intermediate to delayed** onset, **moderate** induction/precipitation of HF
Diltiazem, Verapamil	• Negative inotropic effects • **Immediate to intermediate** onset, **major** induction/precipitation of HF
Nifedipine	• Negative inotropic effects • **Immediate to intermediate** onset, **moderate** induction/precipitation of HF

Recreated from Table 13 from the 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

Abbreviations

ACEi: angiotensin-converting enzyme inhibitors
ARB: angiotensin (II) receptor blocker
ARNi: angiotensin receptor-neprilysin inhibitors
BB: beta-blocker
BNP: B-type natriuretic peptide
BP: blood pressure
CVD: cardiovascular disease
eGFR: estimated glomerular filtration rate
GDMT: guideline-directed medical therapy
HF: heart failure
HFimpEF: heart failure with improved ejection fraction
HFmrEF: heart failure with mildly reduced ejection fraction
HFpEF: heart failure with preserved ejection fraction
HFrEF: heart failure with reduced ejection fraction
LV: left ventricular
LVEF: left ventricular ejection fraction
MI: myocardial infarction
MRA: mineralocorticoid receptor antagonist
NT-proBNP: N-terminal prohormone of B-type natriuretic peptide
NYHA: New York Heart Association
PRN: as needed
PUFA: polyunsaturated fatty acid
RAASi: renin-angiotensin-aldosterone system inhibitor
SGLT2i: sodium-glucose cotransporter-2 inhibitor
T2DM: type 2 diabetes mellitus

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